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IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF NEW YORK

IN RE PFIZER INC. SECURITIES LITIGATION	:	04 Civ. 9866 (RO) (Electronically Filed)

PLAINTIFFS' REPLY MEMORANDUM OF LAW
IN FURTHER SUPPORT OF THEIR MOTION TO STRIKE

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Plaintiffs[1] submit this Reply Memorandum of Law In Further Support of their Motion to Strike Certain Exhibits Attached To The Declaration Of Gregory A. Markel (the "Markel Declaration") And Related Portions Of The Memorandum Of Law In Support Of Defendants' Motion To Dismiss (the "Motion to Strike" or "Pls. MTS").

INTRODUCTION

Defendants' submission of Markel Exhibits 1 and 1A (and their attempt in connection with their reply papers to submit Supplemental Markel Exhibits 45, 48 and 49),[2] clearly violate well-settled principles governing the proper scope of a Rule 12(b)(6) motion to dismiss.

In addition to the violation of Rule 12(b)(6), Defendants' Markel Exhibit 1 (comprised of excerpts from the materials submitted to the FDA including a draft label for Bextra), is comprised of selected pages from a larger confidential document (77 pages out of a document numbering approximately 5,000 pages) that should be stricken as unfair under FED. R. EVID. 106. In their opposition to Plaintiffs' motion to strike ("Def. Opp'n"), Defendants do not cite to a single case where the Defendants were permitted to submit ***excerpts*** of a confidential document. Thus, the arguments Defendants make in their brief related to Exhibit 1 (including Defendants' arguments relying on the Pfizer-drafted proposed label for Bextra) also should be stricken.

Markel Exhibit 1A, a "Primer On Statistical Significance," should likewise be stricken, at least to the extent the Defendants argue that it supports judicial notice that a 5% probability is "statistically significant" as a matter of law. The Primer itself states that the 5% threshold is "wholly arbitrary" and "could just as easily be 10% or 1%." *See* Markel Ex. 1A at 3. Moreover,

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[1] Lead Plaintiff The Teachers' Retirement System of Louisiana ("Lead Plaintiff" or "TRSL"), Named Plaintiffs Michael Feitler ("Feitler"), Christine Fleckles ("Fleckles") and Paul Schapka ("Schapka") and the Class are collectively referred to as "Plaintiffs."

[2] In their reply Defendants withdrew Exhibits 2 and 3 and submit Exhibits 48 and 49 as potential substitutes.

no case cited by Defendants holds that there is a generally accepted 5% probability rule as to which the Court could take judicial notice. *See infra* pgs. 12-16. Thus, this exhibit offers no support for Defendants' position that they were entitled to hide the cardiovascular risks -- to the point of increased mortality -- that the CLASS, CABG Trial 35 and the 1999 Study demonstrated. Indeed, when these increased risks were finally revealed, the FDA took action against the drugs that significantly reduced Pfizer's sales and share price. And in Pfizer's own prescribing information for Lipitor, Pfizer used a 2% threshold for statistical significance, highlighting the factual nature of any definition of "statistically significant."

The new Markel Exhibits 48 and 49, which Defendants submitted in connection with the filing of their Reply Brief in Support of their Motion to Dismiss, should not be considered for the basis for which the material is being offered. To argue that the prevalence of arthritis in the United States could somehow exculpate Defendants' fraud is simply a non-sequitor and in any event improper on a Rule 12(b)(6) motion to dismiss.

Finally, new Markel Exhibit 45, submitted in connection with Defendants' Reply Brief, should be stricken. Not only is the submission of a new exhibit improper on a reply, but the entire document relates to evidence for ***effectiveness*** for drugs, a factual matter not addressed in the Complaint. *See infra* pgs. 13-14.

Accordingly, Defendants' Markel Exhibits 1, 1A and new Markel Exhibits 45, 48-49, and the arguments in Defendants' briefs that rely upon those exhibits, should be stricken.

ARGUMENT

I. THE COURT SHOULD NOT CONSIDER DEFENDANTS' MARKEL EXHIBIT 1

A. THE COURT SHOULD NOT CONSIDER THE EXCERPTS OF THE BEXTRA NDA OR THE EXCERPTS OF THE CABG TRIAL REPORT

Defendants concede that "Plaintiffs do not possess a copy of the full Bextra NDA and the CABG Trial Final Report," but nevertheless argue that Defendants' submission of excerpts of these documents in connection with their motion to dismiss is completely proper. Def. Opp'n at 9. Defendants are wrong.

The law in this regard is clear. On a Rule 12(b)(6) motion to dismiss, a district court is subject to strict requirements to "limit itself to facts stated in the complaint or in documents attached to the complaint as exhibits or incorporated in the complaint by reference." *Kramer v. Time Warner Inc.*, 937 F.2d 767, 773 (2d Cir. 1991). When matters outside the pleadings are presented in response to a Rule 12(b)(6) motion, the court may exclude the additional material and decide the motion on the complaint alone or it may convert the motion to one for summary judgment under FED. R. CIV. P. 56 and afford all parties the opportunity to present supporting material. *Id.* The Second Circuit will "strictly enforce the conversion requirement of Rule 12(b) where there is a legitimate possibility that the district court relied on inappropriate material in granting the motion." *See Amaker v. Weiner*, 179 F.3d 48, 50 (2d Cir. 1999). Accordingly, district courts should strike documents and arguments that are outside the scope of the pleading. *See In re OPUS360 Corp. Sec. Litig.*, No. 01 Civ. 2938, 2002 WL 31190157, at *1 n.3 (S.D.N.Y. Oct. 2, 2002) (granting the plaintiffs' motion to strike exhibits on a motion to dismiss); *In re Cree, Inc. Sec. Litig.*, 333 F. Supp. 2d 461, 470-71 (M.D.N.C. 2004) (granting the plaintiffs' motion to strike and refusing to take judicial notice of articles submitted by the defendants in support of their motion to dismiss). A court may only consider documents extraneous to the

complaint in the very limited circumstance "where the complaint 'relies heavily upon its terms and effect,' which renders the document 'integral' to the complaint." *Chambers v. Time Warner, Inc.*, 282 F.3d 147, 154 (2d Cir. 2002).

Here, Defendants rely upon Markel Exhibit 1 to argue that the number of heart attacks and strokes that Bextra users suffered during clinical trials were not "statistically significant" and to claim that Pfizer fully disclosed Bextra's known cardiovascular risks. *See* Def. MTD at 9-11.[3] This factual argument is simply impermissible. *See Kramer*, 937 F.2d at 774 (taking judicial notice of SEC public filings "not to prove the truth of their contents but only to determine what the documents stated.").[4]

To bolster their position, Defendants principally rely on *Cortec Indus., Inc. v. Sum Holding L.P.*, 949 F.2d 42 (2d Cir. 1991), *cert. denied*, 503 U.S. 960 (1992). Def. Opp'n at 6-9. This case, however, avails them nothing. First, while the trial court did decline to strike certain documents used by a defendant in its motion to dismiss, the trial court in *Cortec* expressly stated it did not rely on the content of the documents the defendants submitted in deciding the motion to dismiss. *Id.* at 47-48. Second, the documents the Second Circuit held the lower court could

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[3] References in the form "Def. MTD" are to Defendants' Memorandum of Law in Support of Their Motion to Dismiss the Consolidated Class Action Complaint, filed May 5, 2006.

[4] Arguments by defendants that data alleged by a plaintiff is not "statistically significant" has been rejected by courts at the motion to dismiss stage. In *Roberts v. United States*, 947 F. Supp. 282 (E.D. Tex. 1996), the court stated:

> Furthermore, the defendant argues that Roberts has failed to present statistically significant evidence of a disparate impact. Yet, this is an inappropriate argument to make in support of a motion to dismiss. As discussed above, at issue in a motion to dismiss is the legal sufficiency, not the factual sufficiency of a party's case. The court must accept as true all material allegations in the complaint, as well as reasonable inferences to be drawn from them. Roberts has claimed that the defendant's policy has a disparate impact on women. At this time, the court must accept this factual averment as true.

Id. at 289. *See also Arnold v. City of York*, No. Civ. 4:03-1352, 2004 WL 2331781, at *5 (M.D. Pa. June 28, 2004) (rejecting defendants' argument that plaintiffs' alleged statistics were faulty or unreliable, holding that "the question of whether plaintiffs' statistics . . . are valid must be construed in favor of the plaintiff at this stage in the proceedings.").

have considered in deciding a motion to dismiss (but did not) were a stock purchase agreement, an offering memorandum, and a warrant that plaintiffs either had in their possession or could have possessed (the plaintiffs were parties to the same documents). The documents in *Cortec* thus were fully available to the plaintiffs. *Id.* at 48. In the instant action, the full Bextra application and CABG Trial 35 are still "confidential" and Pfizer has not given Plaintiffs access to those documents in their entirety (which amount to over 5,000 pages).

Third, while Defendants repeatedly quote the dicta in *Cortec* that: "The stock purchase agreement, Bowles' offering memorandum, and the warrant were documents plaintiffs had either in its possession or had knowledge of and upon which they relied in bringing suit" (Def. Opp'n at 6, 9 n.12), they fail to place the statement in context. After the sentence relied upon by Defendants, the Court continued:

> [T]hough the district court, in light of what it viewed as conflicting precedents in this Circuit, declined to consider these exhibits, it could have viewed them on the motion to dismiss because ***there was undisputed notice to plaintiffs of their contents and they were integral to plaintiffs' claim.***

Cortec, 949 F.2d at 48 (emphasis added). Here, in contrast, it is undisputed that Plaintiffs do ***not*** have notice of the contents of Defendants' full Bextra application and CABG Trial 35. Defendants concede that "Plaintiffs do not possess a copy of the full Bextra NDA and the CABG Trial 35 Final Report." Def. Opp'n. at 9. Plaintiffs only have notice of the select portion of those documents that Defendants have chosen to submit (a mere 77 pages of a document consisting of more than 5,000 pages).[5]

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[5] The Second Circuit in *Cortec* expressly referred to "***actual notice***" of "***all the information***" in the exhibit at issue. *Cortec*, 949 F.2d at 48 ("Where plaintiff has actual notice of all the information contained in the movant's papers and has relied upon those documents in framing the complaint the necessity of translating a Rule 12(b)(6) motion until one under Rule 56 is largely dissipated.") As noted previously, Plaintiffs in the instant action do not have actual notice of the lengthy confidential non-public documents Defendants refer to and do not have all the information contained therein, but merely the select information Defendants chose to disclose.

Defendants fail to cite to any case in which the Court relied on defendant-selected excerpts of a "confidential" document where plaintiffs lacked access to the entire document. *See, e.g., Nappier v. Pricewaterhouse Coopers LLP,* 227 F. Supp. 2d 263 (D.N.J. 2002) (Def. Opp'n. at 9) (documents considered by court were submitted in their entirety as exhibits to defendants' motion to dismiss); *Sazerac Co. v. Falk*, 861 F. Supp. 253 (S.D.N.Y. 1994) (Def. Opp'n. at 9) (pre-PSLRA case where a court considered the Share Purchase Agreement which plaintiff, a party to the agreement, brought suit on).

In their motion to dismiss, Defendants cited to several cases to support their use of Exhibit 1.[6] Plaintiffs Motion to Strike demonstrated that none of these cases support consideration of Exhibit 1 in connection with Defendants' motion to dismiss. Pls. MTS at 16-18. In response, Defendants merely state -- oddly -- that "Plaintiffs' argument that [the *Kramer, Wellbutrin* and *Chan* cases] do not support the consideration of the disputed exhibits is misguided." Def. Opp'n at 10 n.13. Inasmuch as Plaintiffs set forth in detail how inapposite these cases are, it is hardly a convincing argument for Defendants in their opposition to summarily state in response merely that "Defendants cited [these cases] as support." *Id.*

Defendants' primary new case is *In re Bayer AG Sec. Litig.*, No. 03 Civ. 1546 (WHP), 2004 WL 2190357, at *9 (S.D.N.Y. Sept. 30, 2004). *See* Def. Opp'n at 10-12. *Bayer*, however, offers no support to Defendants. *Bayer* merely involved a decision by the court to look at an entire document where that document was cited in and was integral to the complaint in that case. *Id.* at *1 n.1, *11. As noted previously, the Disputed Exhibits upon which Defendants would have this Court rely were neither cited in nor integral to the Complaint.

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[6] *See* Def. MTD at 2 n.3 (citing *Kramer v. Time Warner, Inc.*, 937 F.2d 767 (2d Cir. 1991); *Chan v. Orthologic Corp.*, No. Civ. 96-1514, 1998 WL 1018624 (D. Ariz. Feb. 5, 1998); *In re Wellbutrin Sr/Zyban Antitrust Litig.*, 281 F. Supp. 2d 751 (E. D. Pa. 2003); *Oxford Asset Mgmt. Ltd. v. Jabaris*, 297 F. 3d 1182 (11th Cir. 2002).

Defendants also seek to argue that it is some how proper to quote just "excerpts" from a document. Def. Opp'n at 13-14. To support this argument, Defendants rely on *In re Vicuron Pharm., Inc. Sec. Litig.*, No. Civ. 04-2627, 2005 WL 2989674 (E. D. Pa. July 1, 2005). Their reliance is misplaced. In *Vicuron*, plaintiffs did not dispute the accuracy or the definitional information of a technical term in two readily-available pharmacology reference materials (including The Merck Manual of Diagnosis and Therapy) and other documents (including publicly-available SEC filings) as to which the court took judicial notice. *Id.* at *3. Here, the materials at issue are not a publicly available reference book and Plaintiffs certainly do object to Defendants' cherry-picking selected pages without any opportunity for Plaintiffs to see the hidden materials.

Defendants also argue that under FED. R. EVID. 106 they have no obligation to provide Plaintiffs with a complete copy of the document, excerpts from which Defendants submitted as Markel Exhibit 1. Def. Opp'n at 13 n.17. Defendants claim *United States v. Jackson*, 180 F.3d 55 (2d Cir. 1999) supports their position. Defendants are wrong. The *Jackson* case involved the extortion attempt of Ms. Jackson and others against the entertainer Bill Cosby. At the criminal trial, the court admitted into evidence part of a tape recording of the telephone conversation between one of the defendants (Medina) and Ms. Jackson's father. Unlike the circumstances there, both the objecting defendant Medina and the Court had access to and had heard the full tape recording. The trial court held there was little value to playing the full tape to the jury *after listening to the tape*. *Id.* at 73. In contrast, here Defendants self-servingly state that the thousands of pages Defendants have withheld from Plaintiffs and the Court are "irrelevant" based on Defendants' view alone, and Defendants conclude that "no unfairness can result" from their cherry picking. Def. Opp'n at 13. *United States v. Yevakpor*, 419 F. Supp. 2d 242, 250

(N.D.N.Y. 2006) (excluding government's evidence of three one-minute video segments that were incomplete under FED. R. EVID. 106, finding "the Government's self-selection of material is more prejudicial than probative."); *United States v. Peeples*, No. 01 CR 496, 2003 WL 57030, at *3 (N.D. Ill. Jan. 7, 2003) (requiring the admission of both self-inculpatory and self-exculpatory statements by defendant to insure that defendant's statements will not be misrepresented by the trier of facts); *Chesler v. Trinity Indus., Inc.*, No. 99 C 3234, 2002 WL 1822918, at *3 (N.D. Ill. Aug. 8, 2002) (providing that a police report, including conclusions about the cause of an accident, was admissible but must be admitted in its entirety under the rule of completeness).

Neither the *Vicuron* nor *Jackson* case offer support to Defendants' attempt to use cherry-picked pages from a confidential document (Markel Exhibit 1) or attempt to use the disputed 5% threshold Defendants argue is required by the "Effective Clinical Practice Primer" (Markel Exhibit 1A) (notwithstanding the statement in the Primer that a 5% "threshold is wholly arbitrary" and that "there is nothing magical about a 5% chance").

B. THE COURT SHOULD NOT CONSIDER ANY ARGUMENT THAT THE WARNINGS IN THE DRAFT BEXTRA LABEL WERE WITHHELD FROM THE PUBLIC BY THE FDA

Defendants argue in their reply brief, relying on Markel Exhibit 1, that a Pfizer-drafted proposed label for Bextra, which cautioned that post-CABG patients may have an increased risk of adverse cardiovascular events, should be accepted as an exhibit to support an argument that "Pfizer was required by law to use the label as approved by the FDA without alteration." Def. MTD Reply at 31.[7] Defendants further ask the Court to accept their speculation that "The FDA may have decided not to include [the cautionary statements concerning adverse events in

[7] Defendants also claim (falsely) that: "It also cannot be disputed that Pfizer was required by law to use the [Bextra] label as approved by the FDA without alteration." Def. MTD Reply at 31.

connection with post-CABG patients] because [the FDA] did not approve Bextra for use in treating pain." Def. MTD Reply at 31, n.56, and Def. MTD at 46.

First, this argument is wholly improper since, on a motion to dismiss, Defendants' speculation as to how the cautionary statements in the Bextra label may have been removed is wholly outside the pleadings and is contrary to the rule that all possible inferences be made in plaintiff's favor. *See In re Philip Servs. Corp. Sec. Litig.*, 383 F. Supp. 2d 463, 474 n.6 (S.D.N.Y. 2004); *In re Initial Public Offering Sec. Litig.*, 241 F. Supp. 2d 281, 332 (S.D.N.Y. 2003). Second, Defendants made many fraudulent misrepresentations that have nothing to do with Bextra's label regarding the cardiovascular safety of Bextra. *See* ¶¶ 2, 178, 181, 184, 186-87, 191-93, 195, 198-99, 202, 206, 211, 213-14, 216-18, 221, 226-31.[8] Defendants have gone as far as to state publicly that "Bextra's cardiovascular safety profile [was] well established in long-term studies." ¶ 206. *See also* ¶ 178 ("the use of Bextra at the recommended dose has not been associated with any increased risk of cardiovascular or renal complications …."); ¶ 187 (underscoring Bextra's "improved … cardiovascular safety profile."). Defendants are not permitted to fraudulently misrepresent Bextra as a risk-free painkiller and then hide behind the FDA and documents purportedly submitted to the FDA that never became public. Defendants became obligated to speak accurately about Bextra's safety once Defendants chose to publicly discuss the drug's safety profile. *See Caiola v. Citibank, N.A.*, 295 F.3d 312, 331 (2d Cir. 2002) (choosing to speak creates a duty to speak truthfully); *Fogarazzo v. Lehman Bros., Inc.*, 341 F. Supp. 2d 274, 294 (S.D.N.Y. 2004) (a "half-truth" as that omits "some material fact" can be misleading).

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[8] Citations is the form "¶ ___" are to the Complaint.

Moreover, Defendants' claim (Def. MTD Reply at 31) that "Pfizer was required to use the [Bextra] label as approved by the FDA without alteration" is legally unsupportable. *See Madden v. Wyeth*, No. 3-03-CV-0167-BD, 2005 WL 2278081, at *3 n.6 (N.D. Tex. Sept. 14, 2005) (rejecting "defendant's argument that its warning label is adequate because it was approved by the FDA. Federal regulations do not prohibit a manufacturer from 'add[ing to] or strengthen[ing] a contraindication, warning, precaution, or adverse reaction.'").

Any suggestion that Pfizer could not have changed the FDA-approved Bextra label is false and misleading as a matter of law. The Food, Drug and Cosmetic Act (the "Act") expressly required Pfizer immediately to inform the public of any dangers rather than waiting for the FDA to act. *See* Labeling and Prescription Drug Advertising: Content and Format for Labeling for Human Prescription Drugs, 44 FED. REG. 37434, 37447 (1979); *McEwen v. Ortho Pharm. Corp.*, 528 P.2d 522, 534-35 (Or. 1974). It was, therefore, Pfizer's legal obligation promptly to take steps to strengthen its warnings to the public of any dangers and risks of Bextra (even if the FDA had approved one form of the Bextra label). 21 C.F.R. § 201.57(c) (2006).

The intention of the Act is "to protect consumers from dangerous products." *United States v. Sullivan*, 332 U.S. 689, 696 (1948). *See also FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120 (2000). Consistent with its purpose, the FDA and its regulations explicitly permit a manufacturer unilaterally to strengthen a warning label at any time without regulatory approval, 21 C.F.R. § 314.70(c)(6)(iii)(A), and to allow the drug manufacturer immediately to strengthen warnings when evidence of adverse side effects, risks, or dangers are discovered. *See* 30 FED. REG. 993 (Jan. 30, 1965). *See also McNellis v. Pfizer Inc.*, No. 05-1286-JBS, 2005 WL 3752269, at *7 (D. N.J. Dec. 29, 2005) (the district court, after outlining 21 C.F.R. § 314.70(c)(6), acknowledged a manufacturer's unilateral duty to warn); *Caraker v. Sandoz*

Pharm. Corp., 172 F. Supp. 2d 1018, 1033-34 (S.D. Ill. 2001) (finding that the manufacturer was explicitly authorized by the FDA's regulations to add or strengthen its warnings without prior FDA approval); *Jamison v. Purdue Pharma. Co.*, 251 F. Supp. 2d 1315 (S.D. Miss. 2003) (listing situations where company may amend labeling without prior approval, including "adding or strengthening". . . "a contraindication, warning, precaution, or adverse reaction").[9]

Federal and state courts routinely find that FDA regulations do not impose any restrictions on a drug manufacturer's ability to add warnings or precautions regarding newly-discovered risks and dangers. *See, e.g., Witczak v. Pfizer Inc.*, 377 F. Supp. 2d 726, 729 (D. Minn. 2005) (district court held FDA regulations explicitly permit pharmaceutical companies to unilaterally strengthen the warning label at any time without regulatory pre-approval) (citing 21 C.F.R. § 314.70(c)(6)(iii)(A)). The *Witczak* court noted that the "particular regulation was promulgated precisely to allow drug-makers to quickly strengthen label warnings when evidence of new side effects are discovered." *Id.* (citing 30 FED. REG. 993 (Jan. 30, 1965)). FDA regulation "'permits the addition to the drug's labeling or advertising of information about a hazard without advance approval' by the FDA." *Id.*

In *Cartwright v. Pfizer Inc.*, 369 F. Supp. 2d 876 (E.D. Tex. 2005), Pfizer claimed that plaintiff's state law failure to warn claims were preempted because under the Act because the manufacturer was required to obtain FDA approval before revising the product labeling. The district court specifically rejected this argument:

> Since 1965, the FDA's regulations permit a manufacturer "[t]o add or strengthen a contraindication, warning, precaution, or adverse reaction," without prior approval by the FDA . . ."*(citing* 21 C.F.R. § 314.70(c)(6)(iii)(A) and finding that the Act sets minimum

[9] Similarly, 21 C.F.R. § 201.57(c)(6)(i) states: "labeling must be revised to include a warning . . . ***as soon as there is reasonable evidence of a casual association [of a serious hazard] with a drug; a causal relationship need not have been definitely established.***" (emphasis added).

> standards that "expressly do not prohibit a manufacturer from 'add[ing to] or strengthen[ing] a contraindication, warning, precaution or adverse reaction."')
>
> * * *
>
> Thus, FDA's position regarding stronger warnings by drug manufacturers, as expressed through ***its own* regulations**, is that a manufacturer ***could, and should***, provide stronger warnings as soon as such a warning is warranted.

Id. at 882-83 (emphasis added).

The overwhelming majority of federal and state courts have concluded that a manufacturer not only may, but should add or strengthen warnings related to a pharmaceutical drug, without waiting for FDA approval.[10] Federal regulations require that Defendants should have strengthened the precautions and/or warnings contained in the Bextra label as soon as Defendants had actual or constructive knowledge of the increased risk of cardiovascular risks associated with the ingestion of the drug. Defendants failed to do so and the draft Bextra label included in Exhibit 1 (as well as the arguments Defendants make based upon the draft label) should be stricken.

II. THE COURT SHOULD NOT TAKE JUDICIAL NOTICE OF THE DEFINITION OF "STATISTICALLY SIGNIFICANT" OFFERED BY DEFENDANTS RELYING UPON MARKEL EXHIBIT 1A

Defendants argue that the Court may take judicial notice of the definition of "statistically significant" as forth in Markel Exhibit 1A, an anonymous "Primer" published in an American College of Physicians journal entitled "Statistical Significance and *P* Values." Def. Opp'n at 14-16. Defendants argue that their version of the "statistically significant" definition is not subject

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[10] A minority view on the issue of FDA–approved labeling can be found in *Colacicco v. Apotex, Inc.*, No. Civ. 05-05500, 2006 WL 1443357 (E.D. Pa. May 25, 2006) (holding plaintiffs' product liability claims based on the inadequacy of the FDA–approved labeling for Paxil were preempted and granting pharmaceutical companies' motions to dismiss). Plaintiff Colacicco has appealed to the Third Circuit (Docket No. 06-3107).

to reasonable dispute and, therefore, it is proper for the Court to take judicial notice of Markel Exhibit 1A. *Id.* at 14-15. Defendants are wrong as a matter of fact and as a matter of law.

First, Defendants' use of the 5% threshold for determining "statistically significant" evidence is subject to reasonable factual dispute. A determination of "statistically significant" evidence is complex, requiring consideration of differing views and often involves a battle of the experts. *Cf. McNeil-P.P.C., Inc. v. Bristol-Myers Squibb Co.*, 755 F. Supp. 1206, 1217-19 (S.D.N.Y. 1990) (showing that the statistical definition of "carryover" was subject to differing definitions provided by different statistical experts). Indeed, the "Primer" itself states that the 5% threshold "is wholly arbitrary" and "could just as easily be 10% or 1%." Markel Ex. 1A at 3. Further, Supplemental Markel Exhibit 45 also acknowledges that there are other measures of "statistically significant" evidence other than the 5% threshold, depending on the circumstances of a given study. Markel Ex. 45 at 5 n. 5.

Highlighting the factual nature of the definition of "statistical significance," Pfizer's own prescribing label for its blockbuster drug LIPITOR reports adverse reactions with a ***2% threshold*** (not the 5% threshold Pfizer wishes to impose in their motion to dismiss). *See* http://www.lipitor.com/cwp/appmanager/lipitor/lipitorDesktop?_nfpb=true&_pageLabel=prescribingInformation (stating "The [adverse] events in italics occurred in ≥2% of patients and the events in plain type occurred in <2% of patients," and reporting, *inter alia*, chest pain, nausea, bronchitis, arthritis, and hematuria in greater than 2% of patients). Plaintiffs do not contend that the Court should, at this time, consider Pfizer's prescribing information for Lipitor in connection with Defendants' motion to dismiss. The existence, however, of contrary information in Pfizer's own public documents highlights the factual nature of the issue and demonstrates why the Court should not consider Exhibits 1, 1A and 45. In any event, the Pfizer prescribing information for

LIPITOR can be viewed as an admission by Pfizer that there is nothing that makes 5% the "statistical significance" threshold in all cases or as a matter of law.

The language of Markel Exhibits 1A and 45, creates a factual dispute on the appropriate measure for determining "statistically significant" evidence and, therefore, neither Markel Exhibit 1A nor Supplemental Markel Exhibit 45 should be considered on a Rule 12(b)(6) motion to dismiss. *See In re Revlon, Inc. Sec. Litig.*, No. 99 Civ. 10192 (SHS), 2001 WL 293820, at *8 (S.D.N.Y. Mar. 27, 2001) ("[Defendants'] arguments raise disputed issues of fact, which are not resolvable on a motion to dismiss the complaint").[11] Not to be overlooked, the authors of the 1999 Study, which was conducted by Pfizer, clearly found "statistically significant" the high number of patients suffering heart attacks, strokes or other cardiovascular problems while taking Celebrex to treat mild Alzheimer's disease as compared to a placebo group. ¶¶ 94, 135.[12]

In addition, Defendants' argument that the results of the CABG Study are not "significant" is belied by the reaction by the public and the government to the public announcement of those results. Defendants' partial admission that previously undisclosed results of the CABG Study showed an increase in negative cardiovascular events was made in Pfizer's

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[11] Defendants' reliance on *In re Carter-Wallace, Inc., Sec. Litig.*, 220 F.3d 36 (2d Cir. 2000) in support of this argument (Def. Opp'n at 14-16) is wholly misplaced for the reasons extensively set forth in Plaintiffs Memorandum of Law in Opposition to Defendants' Motion to Dismiss the Consolidated Class Action Complaint (at 16-17, 20 n.15, 23).

[12] Defendants' reliance on *Nix v. Hedden*, 149 U.S. 304 (1893), for the proposition that courts generally take judicial notice of definitions in standard referenced works (Def. Opp'n at 14), is misplaced. *Nix*, unlike the case at bar, did not involve a definition that was subject to differing views. In *Nix*, the Supreme Court took judicial notice of the terms "fruit" as distinguished from "'vegetables' in common speech, or within the meaning of the [T]ariff [A]ct." *Id.* at 306-07. Moreover, two other cases relied upon by Defendants took judicial notice of a definition where plaintiffs did not object to that definition. *See, e.g., Vicuron*, 2005 WL 2989674, at *3 (taking judicial notice of "excerpts discussing the technical term 'volume of distribution' from two reference materials" because "[p]laintiffs [did] not dispute the accuracy of the reference texts or the definitional information."); *Savings Bank Life Ins. Co. of Mass. v. SBLI USE Mut. Life Ins. Co.*, No. Civ. A. 00-3255, 2000 WL 1758818, at **12-13 (E.D. Pa. Nov. 29, 2000) (taking judicial notice of the term at issue where "Plaintiff was well aware of Defendant's use of the term ... for many years and never objected to it."). In contrast, in the instant action, Plaintiffs do dispute the accuracy of the "statistically significant" definition offered by Defendants on a Rule 12(b)(6) motion to dismiss.

October 15, 2004 press release. Markel Supplement Decl. Ex. 46. The release hit the wire at 8:01 a.m. on October 15, 2004 causing a 2% drop on the day of the announcement, from $29.08 to close at $28.50. This stock drop amounts to a market cap loss of ***$4.379 billion***. It cannot seriously be argued that a market cap loss of $4.379 billion is not material. *See In re Burlington Coat Factory Sec. Litig.*, 114 F.3d 1410, 1425 (3d Cir. 1989) ("[i]n the context of an "efficient" market, the concept of materiality translates into information that alters the price of the firm's stock") (Alito, J.).

Furthermore, the FDA took action once the adverse (if not fatal) effects associated with Celebrex and Bextra (primarily from the CLASS, CABG Trial 35 and the 1999 Study) started to become public. ¶¶ 137-147. On April 7, 2005, upon urging from the FDA, Pfizer withdrew Bextra from the market and agreed to insert a "black box" warning in Celebrex's label highlighting the potential for increased risk of cardiovascular events and gastrointestinal bleeding associated with Celebrex use. ¶¶ 141, 146. Other than removing a drug from the market, a "black box" warning is the most potent warning in the FDA's arsenal, used only in the most serious cases (typically those that may lead to death or serious bodily injury). ¶ 140. *See also* 21 C.F.R. § 201.57(c)(1) (requiring a "black box" warning for drugs which have problems "that may lead to death or serious injury ...."); *Witczak*, 377 F. Supp. 2d at 728 (stating that the black-box warning [is] "the most serious kind-warning" imposed by the FDA). These warnings must be prominently displayed in the drug's labeling, thereby informing the public of the drug's risks. ¶ 140. *See also* 21 C.F.R. § 201.57(c). The FDA would not have taken such serious action if the adverse cardiovascular events associated with Celebrex and Bextra were not material and were previously known by the public. Indeed, the FDA prompting Pfizer to withdrawal Bextra from the market and insert a "black box" label for Celebrex is the best

evidence that the adverse findings of the CLASS, CABG Trial 35 and the 1999 Study were "statistically significant." *Oran v. Stafford*, 226 F.3d 275, 286 (3d Cir. 2000) (providing that FDA action is indicative of "statistically significant evidence establishing a serious health risk.").

Finally, Supplemental Markel Exhibit 45, submitted in connection with Defendants' Reply Brief should also be stricken. Not only is the submission of a new exhibit improper on a reply, *Selby v. Principal Mut. Life Ins. Co.*, No. 98-5283 (RLC), 2000 WL 1863760, at *4 (S.D.N.Y. Dec. 20, 2000) (collecting cases and concluding that it is generally improper to present new exhibits and facts in a reply brief) (citations omitted), but the entire document relates to evidence for ***effectiveness*** for drugs (even an ineffective drug may show improvement in a clinical trial and this may result in false positive findings, thus independent substantiation is required). This is a clear factual issue that should not be addressed at this time. *Revlon*, 2001 WL 293820, at *8 (arguments which raise disputed issues of fact are not resolvable on a motion to dismiss).

III. DEFENDANTS' ATTEMPT TO HAVE THIS COURT CONSIDER SUBSTITUTE MATERIAL REGARDING ARTHRITIS SHOULD BE DENIED

Defendants withdrew Markel Exhibits 2 and 3 and, instead, request that the Court consider Supplemental Markel Exhibits 48 and 49. Def. Opp'n at 16-17. Supplemental Markel Exhibit 48 is a Joint Press Release issued by Pfizer and Pharmacia on February 22, 2000, and Supplemental Markel Exhibit 49 is a Joint Press Release issued by Pfizer and Pharmacia on November 19, 2001. Like Markel Exhibits 2 and 3, each of these exhibits highlight the prevalence of arthritis in the United States and explain the various types of arthritis. Defendants' request for the Court to consider Supplemental Markel Exhibits 48 and 49 must be rejected for one of the primary reasons Markel Exhibits 2 and 3 should not be considered -- Defendants are simply taking "snippets" of these press releases to suggest that their fraudulent

misrepresentations and omissions about the cardiovascular safety of Celebrex and Bextra are warranted given the prevalence of arthritis affecting Americans. *See* Pls. MTS at 18-19. This is wholly improper on a Rule 12(b)(6) motion to dismiss.

CONCLUSION

For the foregoing reasons, Plaintiffs' Motion to Strike should be granted.

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Respectfully submitted,

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